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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RINAUDO, JO ANN S	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/823,253	REED, JENNIFER LYNNE	
	Examiner	Art Unit	
	Jo Ann Rinaudo	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-87 and 101-110* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-87 and 101-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-87 and 101-110 are pending.

2. Applicant's election of Group I (claims 1-87 and 101-110) in the reply filed on 5 October 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Applicant has further elected the species of antibody, 7F3com-2H2. Applicant provides the following SEQ ID NOS corresponding to 7F3com-2H2: (1) SEQ ID NO:43, corresponding to the heavy chain (V_H Domain); (ii) SEQ ID NO:47, corresponding to the light chain (V_L Domain); (iii) SEQ ID NO:44, corresponding to the heavy chain CDR1; SEQ ID NO:45, corresponding to the heavy chain CDR2; and SEQ ID NO:46, corresponding to the heavy chain CDR3; and (iv) SEQ ID NO:48, corresponding to the light chain CDR1; SEQ ID NO:49, corresponding to the light chain CDR2; and SEQ ID N0:50, corresponding to the light chain CDR3.

4. The species of antibody, 7F3com-2H2, does not share a substantial structural similarity with the other specific antibodies recited in the claims. Therefore the election of species of antibody, 7F3com-2H2 is based on linking claim practice and not on Markush practice.

5. Claims 1-87 and 101-110 read on the elected species.

6. Claims 1-87 and 101-110 are under consideration as they are drawn to the IL-9 antibody, 7F3com-2H2 comprising (1) SEQ ID NO:43, corresponding to the heavy chain (V_H Domain); (ii) SEQ ID NO:47, corresponding to the light chain (V_L Domain); (iii) SEQ ID NO:44, corresponding to the heavy chain CDR1; SEQ ID NO:45, corresponding to the heavy chain CDR2; and SEQ ID NO:46, corresponding to the heavy chain CDR3; and (iv) SEQ ID NO:48, corresponding to the light chain CDR1; SEQ ID NO:49, corresponding to the light chain CDR2; and SEQ ID N0:50, corresponding to the light chain CDR3; wherein the antibody can also be human or humanized; conjugated; and the pharmaceutical composition thereof.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

8. Claims 1-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. In Claims 1-87, the use of "7F3com-2H2" renders the claim indefinite because "7F3com-2H2" is a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct biological materials. It is suggested that Applicant amend the claims to recite the accession number of the deposited *E. coli* containing the pMI347 vector encoding the IL-9 monoclonal antibody, 7F3com-2H2.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

11. Claims 1-87, 101 and 102 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

12. It is apparent that the *E. coli* containing the pMI347 vector encoding the IL-9 monoclonal antibody, 7F3com-2H2, is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the *E. coli* containing the pMI347 vector encoding the IL-9 monoclonal antibody, 7F3com-2H2, may satisfy first paragraph. See 37 CFR 1.801-1.809.

13. The specification discloses that the *E. coli* containing the pMI347 vector encoding the IL-9 monoclonal antibody, 7F3com-2H2, has been deposited under the provisions of the Budapest Treaty. An affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney or record over his or her signature, stating that the *E. coli* containing the pMI347 vector encoding the IL-9 monoclonal antibody, 7F3com-2H2, has been deposited under the Budapest Treaty and that the *E. coli* containing the pMI347 vector encoding the IL-9 monoclonal antibody, 7F3com-2H2, *will be irrevocably and without restriction or condition released to the public upon the issuance of a patent* would satisfy the deposit requirement made herein. See 37 CFR 1.808.

14. Claims 1-87, 101 and 102 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) an IL-9 antibody that immunospecifically binds to a human IL-9 polypeptide comprising SEQ ID NO:43 heavy chain (V_H Domain), SEQ ID NO:44 heavy chain CDR1, SEQ ID NO:45 heavy chain CDR2, SEQ ID NO:46 heavy chain CDR3, SEQ ID NO:47, light chain (V_L Domain), SEQ ID NO:48 light chain CDR1; SEQ ID NO:49, light chain CDR2; and SEQ ID N0:50, light chain CDR3; and (ii) an IL-9 antibody, wherein the IL-9 antibody has an association rate constant or k_{on} rate of at least 10^5 $M^{-1}s^{-1}$ (Claim 103); or k_{on} rate is at most 10^{11} $M^{-1}s^{-1}$ (Claim 104); an IL-9 antibody, wherein the antibody has a dissociation rate constant or k_{off} rate of less than about $2x10^{-4}s^{-1}$ (Claim 105), or k_{off} rate is greater than 10^{11} $M^{-1}s^{-1}$ (Claim 106); an IL-9 antibody wherein the antibody has an affinity constant (K_a) of at least 10^7 M^{-1} (Claim 107) or the affinity constant is at most $5x10^{11}$ M^{-1} (Claim 108); and an IL-9 antibody, wherein said IL-9 antibody has dissociation constant (K_d) of less than 10^{-9} M (Claim 109) or dissociation constant is greater than $6x10^{-12}$ M (Claim 110) *does not reasonably provide enablement for* an IL-9 antibody which comprises any number less than 6 CDR's; (Claims 1-87, 101 and 102). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention commensurate in scope with these claims.

15. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the

claim, the amount of direction or guidance provided, the lack of sufficient working examples, and the amount of experimentation required to enable one skilled in the art to practice the invention.

16. It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. Janeway et al. teach that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Rudikoff et al. teach that even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRS, may dramatically affect the antigen-binding function. Further, Rudikoff et al. teach that an alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. Furthermore, the specification provides no guidance for making an antibody exhibits binding to IL-9 other than the IL-9 antibody with SEQ ID NO:43, corresponding to the heavy chain (V_H Domain); SEQ ID NO:47, corresponding to the light chain (V_L Domain); SEQ ID NO:44, corresponding to the heavy chain CDR1; SEQ ID NO:45, corresponding to the heavy chain CDR2; and SEQ ID NO:46, corresponding to the heavy chain CDR3; and SEQ ID NO:48, corresponding to the light chain CDR1; SEQ ID NO:49, corresponding to the light chain CDR2; and SEQ ID N0:50, corresponding to the light chain CDR3. Therefore, the lack of guidance provided, the lack of sufficient working examples, and the amount of experimentation required does not enable one skilled in the art to make and use an IL-9 antibody, as recited in the claims.

17. Reasonable correlation must exist between the claims and the enablement set forth. Without sufficient guidance, knowing only the heavy chain sequence or only the light chain sequence of an antibody results in unpredictable binding specificity of the antibody molecule; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

18. Claims 1-87, 101 and 102 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonable convey to one skilled in the art that the inventor(s), at the time of the application was filed, had possession of the claimed invention.

19. Applicant is in possession of (i) an IL-9 antibody that immunospecifically binds to a human IL-9 polypeptide comprising SEQ ID NO:43 heavy chain (V_H Domain), SEQ ID NO:44 heavy chain CDR1, SEQ ID NO:45 heavy chain CDR2, SEQ ID NO:46 heavy chain CDR3, SEQ ID NO:47, light chain (V_L Domain), SEQ ID NO:48 light chain CDR1; SEQ ID NO:49, light chain CDR2; and SEQ ID N0:50, light chain CDR3; and (ii) an IL-9 antibody, wherein the IL-9 antibody has an association rate constant or k_{on} rate of at least 10^5 $M^{-1}s^{-1}$ (Claim 103); or k_{on} rate is at most 10^{11} $M^{-1}s^{-1}$ (Claim 104); an IL-9 antibody, wherein the antibody has a dissociation rate constant or k_{off} rate of less than about $2x10^{-4}s^{-1}$ (Claim 105), or k_{off} rate is greater than 10^{11} $M^{-1}s^{-1}$ (Claim 106); an IL-9 antibody wherein the antibody has an affinity constant (K_a) of at least 10^7 M^{-1} (Claim 107) or the affinity constant is at most $5x10^{11}$ M^{-1} (Claim 108); and an IL-9 antibody, wherein said IL-9 antibody has dissociation constant (K_d) of less than 10^{-9} M (Claim 109) or dissociation constant is greater than $6x10^{-12}$ M (Claim 110). Applicant is not in possession of an IL-9 antibody which comprises any number less than 6 CDR's; (Claims 1-87, 101 and 102).

20. There is insufficient written description of an antibody that immunospecifically binds to a human IL-9 polypeptide and comprises less than 6 specific known CDR sequences or heavy chain (V_H Domain) and a light chain (V_L Domain). The specification does not describe sufficient structural and functional characteristics of an antibody that immunospecifically binds to a human IL-9 polypeptide, other than the antibody of SEQ ID NO:43, corresponding to the heavy chain (V_H Domain); SEQ ID NO:47, corresponding to the light chain (V_L Domain); SEQ ID NO:44, corresponding to the heavy chain CDR1; SEQ ID NO:45, corresponding to the heavy chain CDR2; and SEQ ID NO:46, corresponding to the heavy chain CDR3; and SEQ ID NO:48, corresponding to the light chain CDR1; SEQ ID NO:49, corresponding to the light chain CDR2; and SEQ ID N0:50, corresponding to the light chain CDR3. Therefore the skilled artisan cannot envision all the contemplated antibodies that immunospecifically binds to a human IL-9 polypeptide, as recited in the claims.

21. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

22. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

23. Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

25. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

26. Claims 107 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,261,559 (Reference IDS No. A22), in view of Liebman et al.

27. The '559 patent teaches the production of monoclonal and polyclonal antibodies to IL-9 for therapy (see column 14, lines 45-67; and column 15, lines 1-10, in particular).

28. The claimed invention differs from the reference teaching by the recitation of an IL-9 antibody wherein the antibody has an affinity constant (K_a) of at least $10^7\ M^{-1}$ (Claim 107) or the affinity constant is at most $5x10^{11}\ M^{-1}$ (Claim 108).

29. Liebman et al teach that the typical association constants for antibody interactions are in the range of $1x10^5$ to $1x10^8\ M^{-1}$ and can be as high as $10^{12}\ M^{-1}$ (see page 307, paragraph 2, in particular).

30. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the association constants as taught by Liebman et al., for the IL-9 antibodies, as taught by the '559 patent. One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the '559 patent teaches the

production of IL-9 antibodies for therapy, Liebman teach that the typical association constants for antibody interactions are in the range of $1x10^5$ to $1x10^8$ M^{-1} and can be as high as 10^{12} M^{-1}.

31. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in arriving at the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

32. Claims 103-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,261,559 (Reference IDS No. A22), in view of U.S. Patent Publication 2002/0051787.

33. The '559 patent teaches the production of monoclonal and polyclonal antibodies to IL-9 for therapy (see column 14, lines 45-67; and column 15, lines 1-10, in particular).

34. The claimed invention differs from the reference teaching by the recitation of an IL-9 antibody has an association rate constant or k_{on} rate of at least 10^5 $M^{-1}s^{-1}$ (Claim 103); or k_{on} rate is at most 10^{11} $M^{-1}s^{-1}$ (Claim 104); an IL-9 antibody, wherein the antibody has a dissociation rate constant or k_{off} rate of less than about $2x10^{-4}s^{-1}$ (Claim 105), or k_{off} rate is greater than 10^{11} M^{-1} s^{-1} (Claim 106); an IL-9 antibody wherein the antibody has an affinity constant (K_a) of at least 10^7 M^{-1} (Claim 107) or the affinity constant is at most $5x10^{11}$ M^{-1} (Claim 108); and an IL-9 antibody, wherein said IL-9 antibody has dissociation constant (K_d) of less than 10^{-9} M (Claim 109) or dissociation constant is greater than $6x10^{-12}$ M (Claim 110).

35. The '787 publication teaches that antibodies have dissociation constants in the range of 10^{-7}M to 10^{-11}M and that high affinity antibodies have dissociation constants of about 10^{-9}M or lower (see page 3, column 2, paragraph [0037], in particular). Furthermore, the '787 publication teaches that the dissociation constant can easily be converted to the association constant by taking the reciprocal of the dissociation constant and adjusting the units to reciprocal of molar. In addition, the '787 publication teaches that the rate constants for the association and

dissociation reactions can be measured by standard kinetic methodology for antibody reactions. Moreover, the '787 publication teaches that therapeutically effective antibodies include high affinity neutralizing antibodies (see page 3, column 1, paragraph [0034], in particular).

36. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the affinity, association and dissociation rate constants, as taught by the '787 publication, for the IL-9 antibodies, as taught by the '559 patent. One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the '559 patent teaches the production of IL-9 antibodies for therapy, and the '787 publication teaches that therapeutic antibodies are high affinity antibodies, high affinity antibodies have dissociation constants of about 10^{-9}M or lower, and that the affinity of antibodies can be measured by standard kinetic methodology for antibody reactions.

37. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in arriving at the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

38. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

39. No claim is allowed.

40. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jo Ann Rinaudo whose telephone number is 571.272.8143. The examiner can normally be reached on M-F, 8:30AM - 5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571.272.0841. The fax phone number for the organization where this application or proceeding is assigned is 571.273.8300.

41. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jo Ann Rinaudo, Ph.D.
Patent Examiner
11/07/2005

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